VIETNAM NATIONAL UNIVERSITY

UNIVERSITY OF ENGINEERING AND TECHNOLOGY

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DEVELOPMENT OF A PROTEIN DETECTION SYSTEM FOR POINT-OF-CARE TESTING (POCT) IN BIOMEDICAL DIAGNOSTICS

Major: Electronic engineering

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SUMMARY OF DOCTORAL THESIS IN ELECTRONIC ENGINEERING

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Thesis introduction

Background and context of the research

Proteins, composed of amino acid chains linked by peptide bonds, play pivotal roles in the human body. Beyond serving as structural components of cells, they participate in nearly all biological processes, from catalyzing metabolic reactions to regulating the immune response. For instance, proteins help form immune serum (antibodies), which defends the body against infections and pathogens. Due to these critical functions, protein testing has become an essential tool in diagnosing and treating various diseases, particularly cancers.

Currently, several immunoassay-based techniques, such as immunohistochemistry (IHC), enzyme-linked immunosorbent assay (ELISA), and flow cytometry, are used to detect and quantify proteins in clinical settings. These methods, relying on optical measurement, provide high accuracy and specificity and are widely implemented in clinical and research laboratories. However, traditional techniques face challenges such as detection sensitivity limits, extended processing times, and the need for skilled operators, limiting their feasibility for point-of-care testing (POCT) applications. Consequently, researchers are shifting their focus toward developing more adaptable, automated solutions.

Emerging microfluidic and biosensing technologies offer potential solutions to these challenges, with several advantages such as enhanced sensitivity, reduced sample volume, and streamlined workflows. Microfluidic channels, in particular, allow precise sample manipulation and can isolate, concentrate, and analyze biological markers in small volumes, providing an ideal foundation for POCT systems. By integrating biosensors with microfluidic platforms, these systems could effectively replace conventional, lab-bound techniques.

In this study, an automated POCT system that combines biosensors with a microfluidic chip was developed to detect and quantify protein concentration the the solution, offering preliminary diagnostic insights. This system requires minimal user intervention and has the potential to provide rapid, reliable, and accessible diagnostic results, marking an important advancement in the early detection and monitoring of diseases.

Objective and significance of the research:

This dissertation focuses on developing a protein enrichment and detection system, designed to integrate with a microfluidic platform for efficient preconcentration and detection of proteins using minimal volumes and short experiment times. The research objective is to investigate, design, and conduct experiments on the proposed system, utilizing a microfluidic chip based on electrochemical immunosensor principles. The chip detects target proteins in solution by monitoring changes in fluorescence and electrical signals. These output signals are recorded, processed, and displayed, offering a streamlined approach to protein detection and analysis.

Scientific and practical significance:

This research sits at the intersection of multiple fields, including electronics, control systems, microfluidics, physics, biology, and microfabrication. The proposed system aims to detect the presence of specific proteins and quantify their concentrations in solutions. Successfully implementing this system would provide a cost-effective alternative to high-end commercial equipment, enabling rapid protein detection without the need for extensive laboratory infrastructure. Additionally, the system offers on-site detection and quantification, requiring only a short processing time, minimal sample volume, and a straightforward operational process.

Methods and scope of the study:

To achieve the specific objectives, this thesis encompasses several key research components: a comprehensive literature review, system modeling, structural analysis, fabrication processes, and experimental measurements to evaluate system performance. Specifically, the work involves designing a microfluidic structure integrated with preconcentration units and sensing electrodes, as well as modeling and analyzing the system's operation. Additionally, the study focuses on control circuit design, protein preconcentration within the microchannel, and signal processing circuits to accurately detect protein presence in the sensor region.

Overview of the dissertation structure:

The thesis consists of 5 main chapters.

Chapter 1: In this chapter, an overview to protein and the role of protein in the human is presented. Then, the review of protein immunoassay methods is provided. Finally, protein preconcentration principle and methods as well as the theory of ion polarization in nanofluidic channels are given.

Chapter 2: This chapter details the development of a microfluidic chip for protein preconcentration using a dual-gate structure and ion-selective nanomembrane. First, a preconcentrator is designed and modeled to analyze the operation of the structure. Then, the chip fabrication process is outlined, employing photolithography and soft lithography techniques. Finally, experiments are conducted to evaluate the functionality and performance of the proposed chip.

Chapter 3: This chapter describes the development of immunosensors through the electrode surface functionalization process, applied to both gold and carbon electrodes. Fluorescence and electrical measurements are then conducted to detect protein captured on the electrode surface. Additionally, a performance comparison between sensors based on two-electrode and three-electrode configurations is presented, highlighting

the strengths and limitations of each configuration in terms of sensitivity and detection accuracy.

Chapter 4: This chapter presents the development of a pre-concentration control system and an electrochemical measurement circuit. First, the system's design and block diagram are introduced to outline its functional components and workflow. Following this, the embedded algorithms and graphical user interface (GUI) are described, detailing their roles in system operation and user interaction. Finally, experimental tests are conducted to evaluate the system's performance, verifying its effectiveness in pre-concentration control and electrochemical measurement.

Chapter 5: In this chapter, the development of integrated microfluidic chip for protein concentration and detection has been presented. First, the chip design is introduced, providing an overview of its operation and functional layout. Following this, the fabrication processes for the electrode and microchannel structures are presented. Finally, a series of experiments are conducted to evaluate and verify the chip's performance, assessing its efficiency in protein concentration and detection.

Finally, the author concludes the research and suggests directions for future studies.

Chapter 1. Overview

1.1. Introduction of protein and the role of protein in the body

Protein, also known as polypeptides, is a vital biological molecule composed of multiple amino acids linked by covalent peptide bonds. Proteins play essential roles in cellular processes, including participation in metabolic reactions, DNA replication, response to stimuli, and the transport of molecules from one location to another.

Proteins play an indispensable role in sustaining life and human bodily functions, directly impacting numerous aspects of normal physiology. Accounting for up to 50% of the cell's total dry mass,

proteins serve not only as crucial structural components but also actively participate in the maintenance, repair, and growth of the body. In medicine and biological research, proteins are regarded as essential biomarkers, aiding in the identification and diagnosis of various diseases as well as in monitoring their progression.

1.2. Protein immunoassay methods

Protein testing primarily relies on immunoassays with various techniques, including:

- Immunohistochemistry (IHC)
- Enzyme Linked Immunosorbent Assay (ELISA)
- Flow cytometry
- Protein microarrays
- Lab-on-a-chip system

1.3. Protein preconcentration and protein preconcentration methods

Although polymerase chain reaction (PCR) is a powerful and widely used technique for the exponential amplification of specific DNA or RNA sequences, it is not directly applicable to the amplification of proteins. To address these challenges, various methods have been developed to enrich or amplify specific proteins from complex biological samples, including:

- Electrokinetic trapping
- Field amplification stacking (FAS)
- Isotachophoresis
- Isoelectric focusing
- Micellar electrokinetic sweeping
- Chromatographic preconcentration

These techniques aim to control and increase the local concentration of proteins near the biosensor surface, making even low-abundance biomarkers detectable.

1.4. Electrostatic interaction and ion concentration polarization in nanofluidic channels

The electric double layer (EDL) plays an increasingly significant role in determining physical properties such as ion selectivity, viscosity, and proton mobility within a nanofluidic channel. When a solid surface contacts a liquid electrolyte, it acquires a surface charge, attracting a layer of oppositely charged ions (counterions) at the interface. This initial layer, known as the Stern layer, is closely bound to the surface. Due to their high surface area-to-volume ratio, nanochannels with a sufficiently large Debye length can have the EDL occupy most of the channel volume. As a result, nanochannels can preferentially transport counterions (opposite to the surface charge), leading to unique physical effects such as ion concentration polarization (ICP).

Chapter 2. Development of a microfluidic chip for protein preconcentration using dual gate structure and ion-selective nanomembrane

2.1. Materials and apparatuses

Some materials and apparatuses were used to fabricate microfluidic chips and investigate the working modes of the preconcentrator.

2.2. Chip design and operational principle

The proposed preconcentration structure was designed with a dual-gate configuration, including three micro-channels of a main channel in the middle and two symmetrical sub-channels (Figure 2.1 (a)).

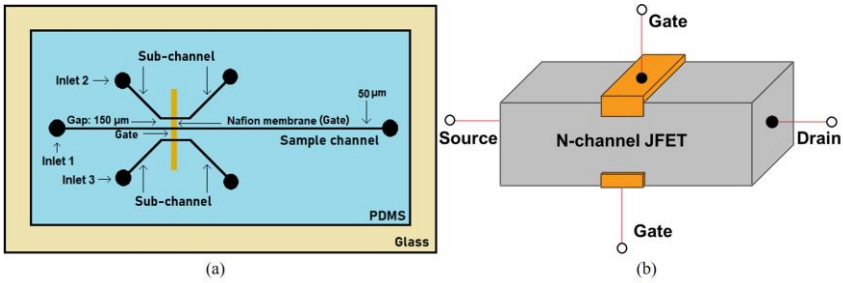


Figure 2.1. (a) Design of protein preconcentration chip with a dual-gate structure; (b) Equivalence diagram of the structure as an N-channel JFET component

The sub-channels were electrically connected to the main channel through an ion-selective membrane formed from the Nafion solution. The term gate represents the nanomembrane (nanojunction) between the main channel and the sub-channel. The proposed structure can be modeled as an N-channel Junction Field Effect Transistor (JFET), a common semiconductor device in electronic circuits, as shown in Figure 2.1 (b).

The proposed preconcentration procedure includes depletion and enrichment modes, as shown in Figure 2.2 (a) and (b).

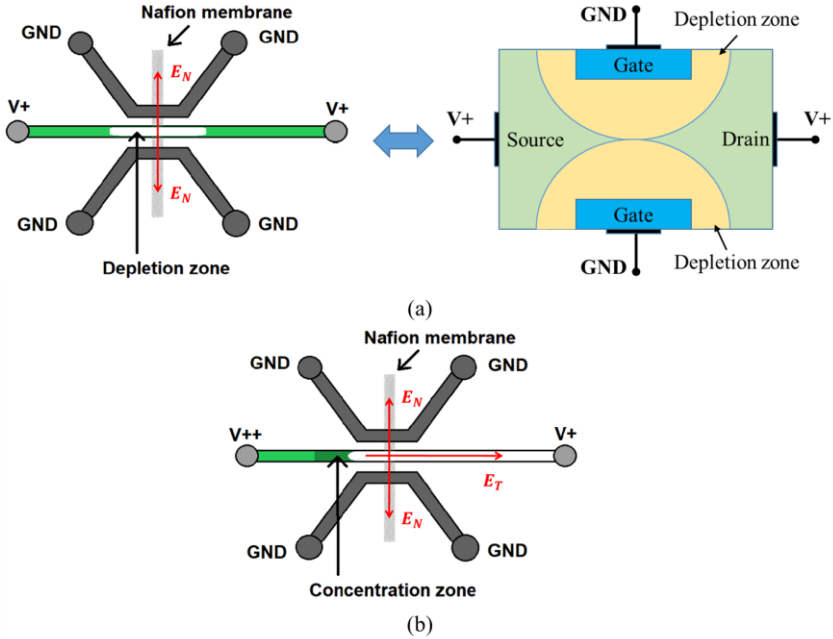


Figure 2.2. Operation principle of proposed preconcentrator with two modes: depletion (a) and enrichment (b).

2.3. Chip fabrication

The fabrication process of the proposed chip consisted of 12 steps combining the soft-lithography technique and the micro-flow patterning technique, as shown in Figure 2.3.

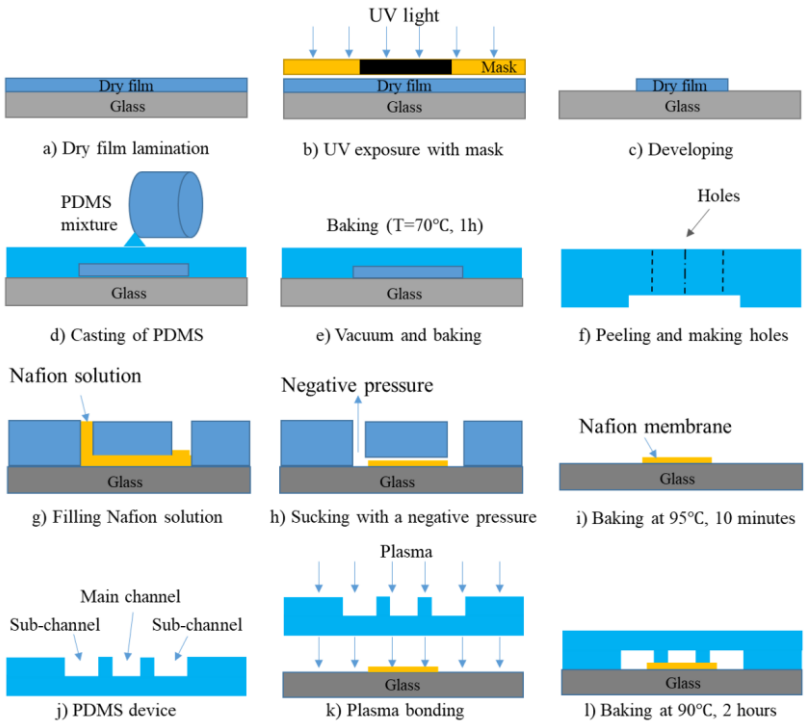


Figure 2.3. Fabrication process of the proposed structure using soft-lithography and micro-flow patterning techniques

2.4. Results and Discussions

An inverted microscope system integrated with a high-speed camera was used to observe and record the fluorescence image of the microfluidic channel. A personal computer coupled with PCC software from Vision Research Company was connected to a high-speed camera for data acquisition and analysis.

2.5. Results and Discussions

Figure 2.5 shows the result of the depletion mode. The fluorescence signal at the middle region of the main channel, where the Nafion membrane was patterned for electrical connection between the sub-channels and the main channel, decreased significantly, called the

depletion zone. his can be explained that the BSA protein molecules and anions were repelled from the depletion region and moved to the two ends of the main channel due to the impact of electrophoresis force (EPF).

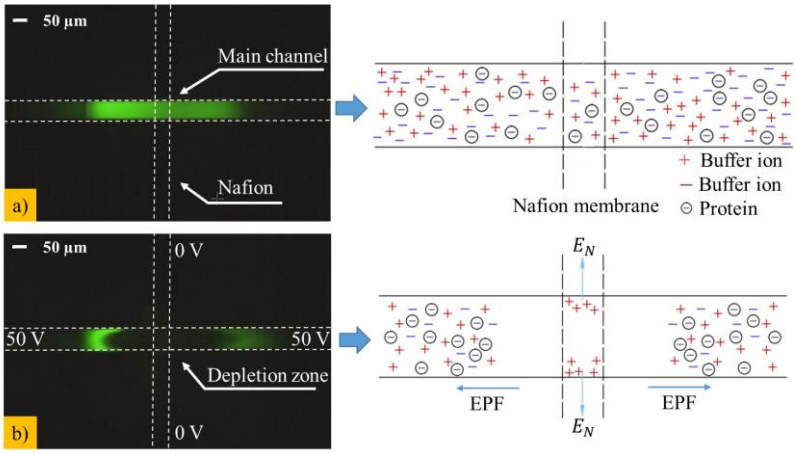


Figure 2.5. Depletion zone concentration result. (a) Before applying voltages; (b) After 20 seconds of applying a voltage of 50 V at the two ends of the main channel and 0 V at the two ends of each sub-channel.

In the enrichment mode, the higher voltage region of the main channel in front of the depletion zone exhibited a higher fluorescence signal intensity. In comparison, the lower voltage region of the channel demonstrated a decrease in the fluorescence signal, as shown in Figure 2.6.

In this study, five BSA protein concentrations were used to quantitatively evaluate the proposed chip's preconcentration factor and speed. Fluorescence intensity was represented by the mean value of a square measurement window located within the protein concentration region, as shown in Figure 2.6. The experimental results indicated that the protein preconcentration speed at the high initial concentration group, including 25 μM and 30 μM, was much faster than the lower initial concentrations (Figure 2.7). For the lower concentration group, the

period for protein preconcentration was markedly lower.

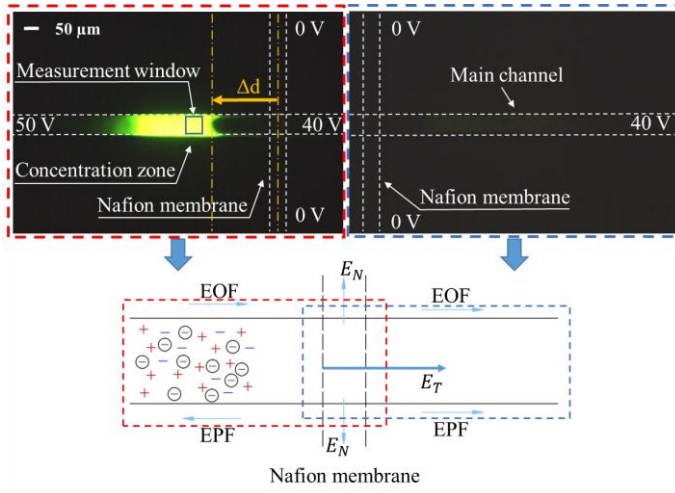


Figure 2.6. Protein preconcentration results, proteins were accumulated in the concentration zone.

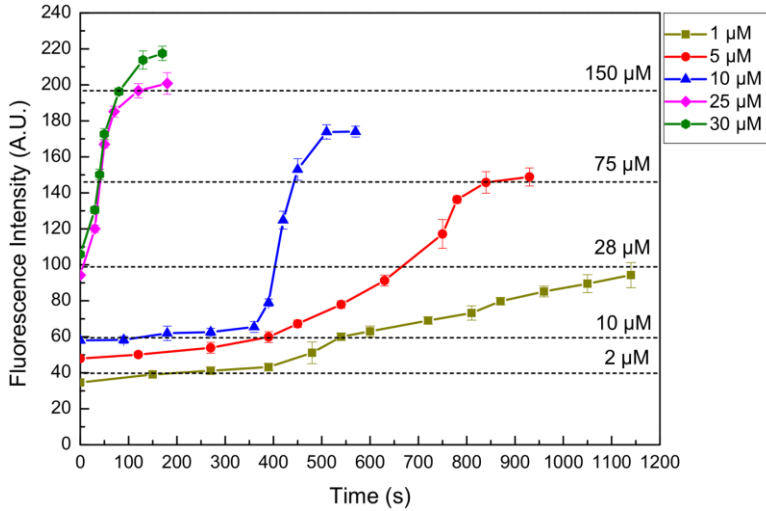


Figure 2.7. The protein concentration increases over time in the concentration zone

Two gold micro-electrodes were integrated into the main channel to measure the impedance of the protein sample after the preconcentration stage. The electrode fabrication process was divided into 6 steps, as shown in Figure 2.10 (a). Figure 2.10 (b) shows the actual image of the gold electrode observed under the microscope. The impedance between two electrodes was measured before and after the protein pre-concentration process. After applying the potentials to the ends of micro-channels, proteins were manipulated and concentrated at the sensing electrode area, as shown in Figure 2.10 (c). Besides, the impedance has been decreased significantly after pre-concentrating protein to the sensing area.

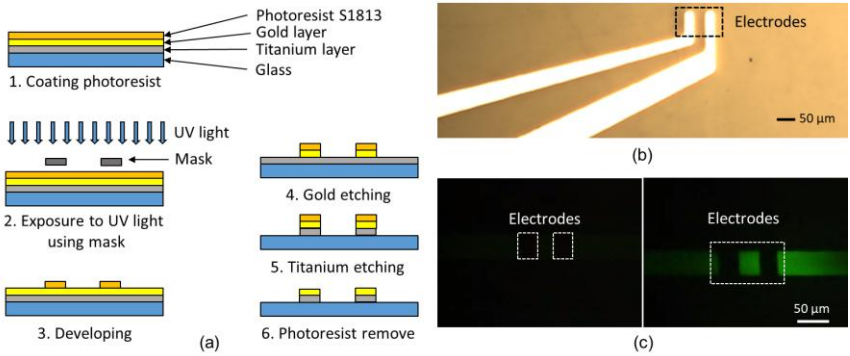
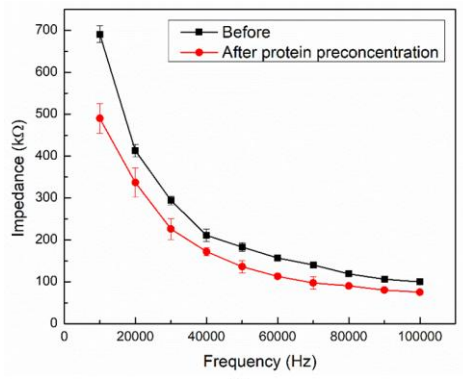
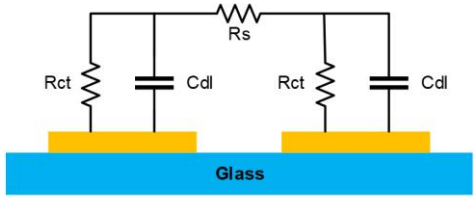


Figure 2.10. (a) The gold electrode fabrication process using photolithography technique; (b) The actual image of the electrode under the microscope; (c) The change of fluorescence signal of electrode area before and after protein pre-concentration in the main channel.

Besides, the impedance has been decreased significantly after pre-concentrating protein to the sensing area, as shown in Figure 2.11 (a). The two impedance curves are clearly separated in the frequency range from 10 kHz to 100 kHz. Besides, the impedance at high frequency range is lower and more stable than low frequency range. These change in the impedance can be explained by the simplified Randles (Figure 2.11 (b)).



(a)



(b)

Figure 2.11. (a) The change of impedance between two electrodes before and after protein pre-concentration; (b) The simplified Randles model was used to explain the impedance change of concentration zone.

Chapter 3. Electrode surface functionalization and development of protein detection immunosensors

3.1. Materials and apparatuses

Chemicals, electrodes and apparatuses were prepared to perform electrode surface functionalization procedures and develop for protein detection.

3.2. The structure of commercial screen-printed electrode

There are three electrodes in a screen-printed gold electrode used in the experiments, including working, counter and reference.

3.3. Gold electrode surface functionalization process

The screen-printed gold electrode surface functionality process was divided into five main steps, as shown in Figure 3.2.

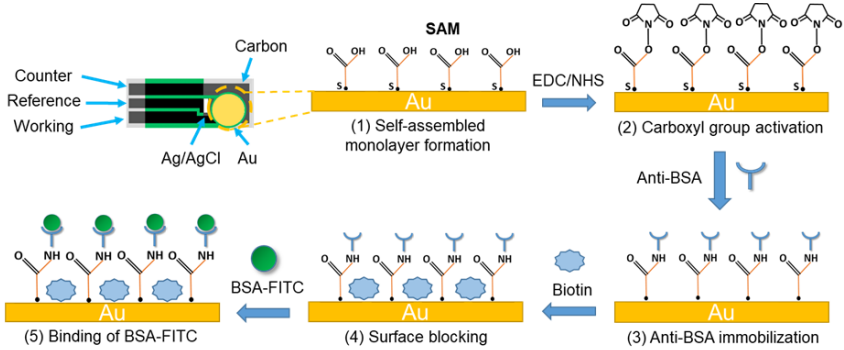


Figure 3.2. The screen-printed gold electrode surface functionality process for immobilizing anti-BSA and detection of BSA

3.4. Carbon electrode surface functionalization process

The screen-printed gold electrode surface functionality process was divided into five main steps, as shown in Figure 3.3.

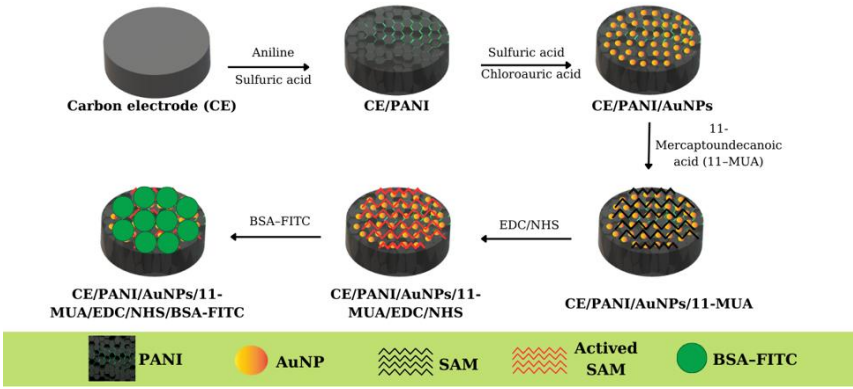


Figure 3.3. Carbon electrode functionalization using aniline and gold nanoparticles

3.5. Results and discussion for gold electrodes

The results obtained include:

- Results of specific binding performance between different electrodes and thiols
- Investigation results of 11-MUA incubation time
- Investigation results of BSA protein concentration
- Investigation results of electrode surface using Raman spectroscopy measurements
- Investigation results using electrical measurements
- Performance comparison results between sensors based on 2-electrode and 3-electrode configurations

3.6. Results and discussion for gold electrodes

The results obtained include:

- Electro-polymerization of aniline on the screen-printed carbon electrode
- Electro-deposition of gold nanoparticles on the electrode surface
- Investigation results of electrode surface morphology
- Electrode surface investigation using fluorescence
- Electrode surface investigation using cyclic voltammetry

Chapter 4. Development of a preconcentration control system and electrochemical measurement circuit

4.1. Materials and apparatuses

Components and chemicals were prepared to fabricate and investigate the operation of the proposed system

4.2. Design and fabrication of electrochemical and impedance measurement circuit

Figure 4.1 shows block diagram of the proposed system, including center processing block, measurement circuit, sensors, and communication. In the center processing block, ESP32 Wi-Fi and Bluetooth module was utilized to configure the parameters and registers of the AD5941 measurement circuit. The system circuit was designed and fabricated using a multi-layer printed circuit board (PCB) technique.

After soldering, the circuits were enclosed within a 3D-printed box fabricated using 3D printing technology

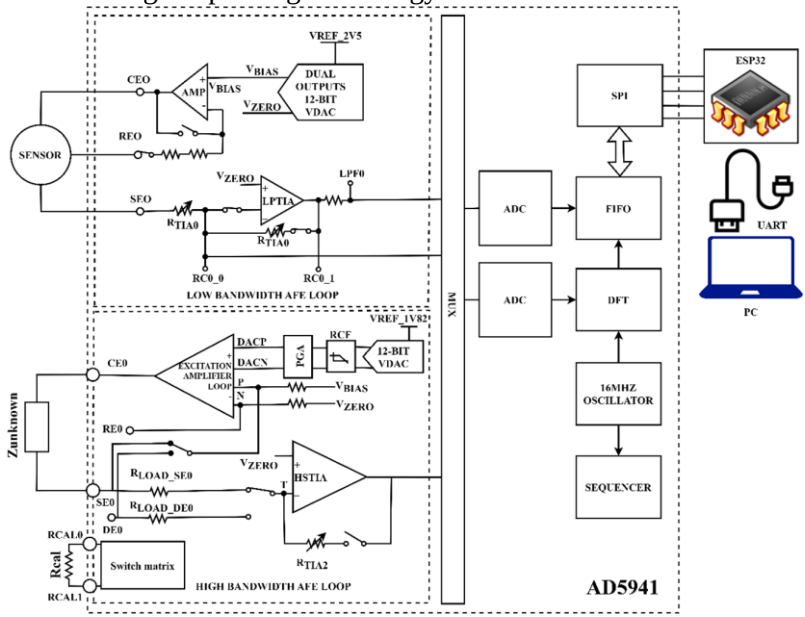


Figure 4.1. Block diagram of the proposed system with 4 main blocks, including processing block, measurement circuit, sensors, and communication

4.3. Design and fabrication of system integrating preconcentrator and electrochemical measurements

The proposed system executed two primary tasks, including protein pre-concentration at low concentrations and employing electrochemical measurement techniques for target protein detection. Figure 4.3 shows shows the overall design and the block diagram of the proposed system. The proposed system was divided into five main blocks, including the central control unit, measurement circuit, voltage controller, bio-chip and graphical user interface (GUI). The central control module utilized the ESP32 DevKit V1 development board, was responsible for automating the testing process.

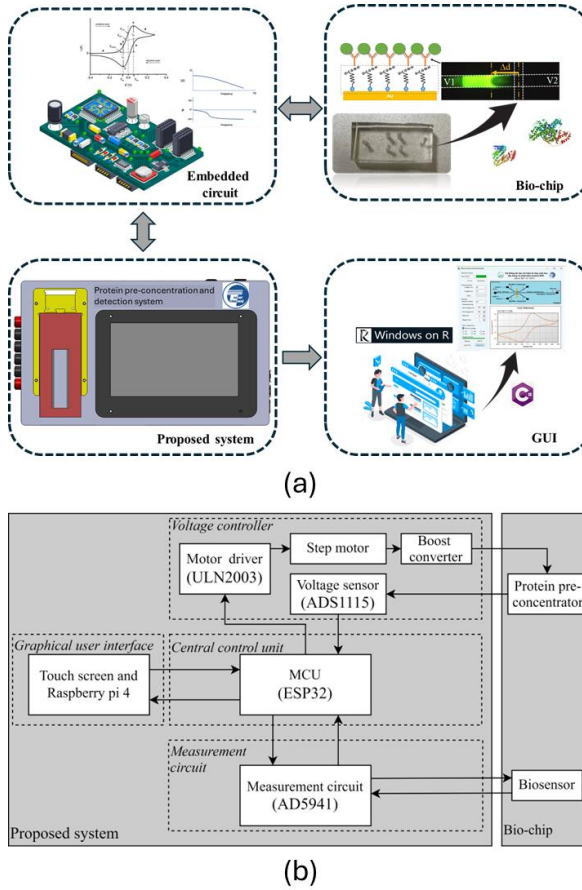
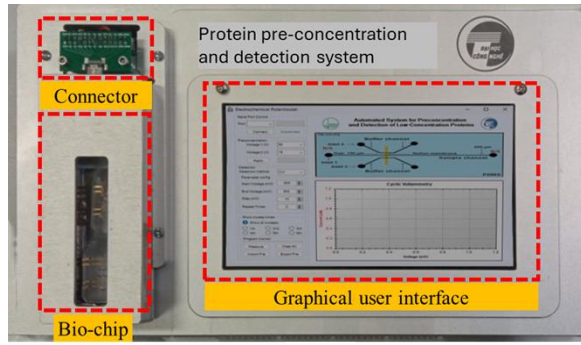
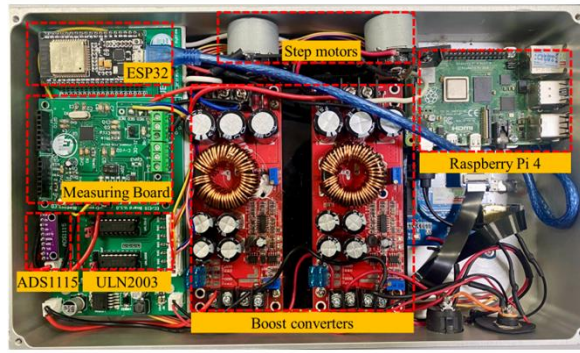


Figure 4.3. System design; (a) Overall design; (b) Block diagram of the proposed system

Figure 4.4 shows the actual images of the proposed system after designing and fabricating. The outside of the proposed system included a bio-chip, connector and graphical user interface (Figure 4 (a)). Within the system, the internal components included a measurement circuit incorporating the AD5941, along with a motherboard facilitating connections among various modules (Figure 4 (b)).



(a)



(b)

Figure 4.4. Actual image of the proposed system after designing and fabricating. (a) Outside the system; (b) Inside the system

4.4. Embedded algorithm on microprocessor and GUI for electrochemical and impedance measurement circuit

There were two algorithms, including:

- Algorithm 1. Firmware for measurements and data acquisition
- Algorithm 2. Software on PC

4.5. Graphical user interface and embedded software for system integrating preconcentrator and electrochemical measurements

The graphic user interface was designed and developed using Visual Studio IDE, a software development environment provided by Microsoft, based in the USA, employing the C sharp programming

language. GUI included a control panel and a graphing area. The control panel contained three functional control groups, including serial port control, pre-concentration and measurement groups.

There were two algorithms, including:

- Algorithm 3. Implementation of the voltage control function
- Algorithm 4. Implementation of the Electrochemical measurement function

4.6. Experimental setup

For the investigation of protein pre-concentration, the protein pre-concentration chip was positioned under the microscope and connected to the system via wires. The voltages were configured on the screen of the device. The protein pre-concentration process was observed on a computer screen connected to the high-speed camera of the microscope system.

4.7. Results and discussion

The experimental results include:

- Investigation of voltage controller
- Investigation of protein preconcentration
- Investigation of CV measurement
- Investigation of impedance spectroscopy measurement

Chapter 5. Development of integrated microfluidic chip for protein concentration and detection

5.1. Materials and apparatuses

Chemicals and apparatuses were prepared to fabricate the microfluidic chip and investigate its operation.

5.2. Electrochemical biosensor design for NSE detection

The proposed biosensor consists of three main electrodes, including working, counter, and reference electrodes, as shown in Figure 5.1. The working and counter electrodes were made of gold-sputtered material, while the reference electrode was made of Ag/AgCl. The working electrode played a crucial role as the site for electrochemical reactions.

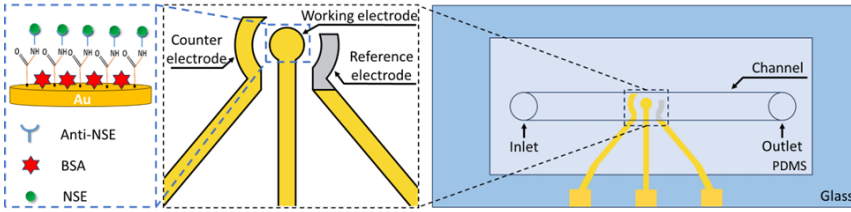


Figure 5.1. Microfluidic chip design, including an electrochemical biosensor integrated inside the miro-channel

5.3. NSE detection Electrochemical biosensor design for BSA pre-concentration and detection

The microfluidic chip design was divided into two main parts, including a protein pre-concentrator and a bioelectrochemical sensor, as shown in Figure 5.2. The protein pre-concentrator had a dual-gate configuration with a main channel in the middle and two symmetrical sub-channels. The two sub-channels were connected to the main channel through a Nafion membrane. The dual gate represented two Nafion membrane layers connecting between the main channel and sub-channels.

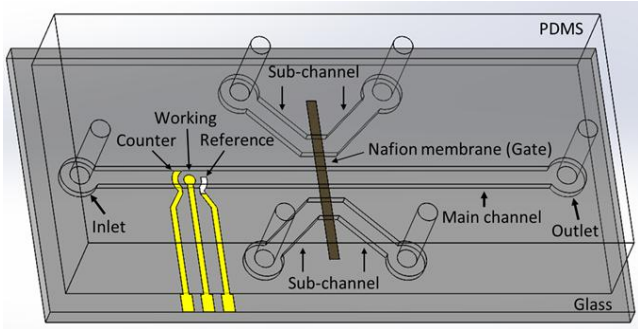


Figure 5.2. Design of the proposed microfluidic chip featuring a protein pre-concentrator and an bioelectrochemical sensor

5.4. Electrochemical Biosensor Fabrication Process

The fabrication process of the electrode structure consists of six main steps, including coating photoresist, exposure to UV light using the mask, developing, gold etching, titanium etching, and photoresist removal. After being fabricated, the gold electrodes were cleaned with

IPA solution, DI water, and nitrogen-dried. Subsequently, the initial three steps in the aforementioned process were reiterated using another mask to selectively expose only the reference electrode, covering the remaining electrodes with a photoresist layerThe fabrication process of the reference electrode involved two phases: silver electroplating and silver chloride coating, as depicted in Figure 5.4.

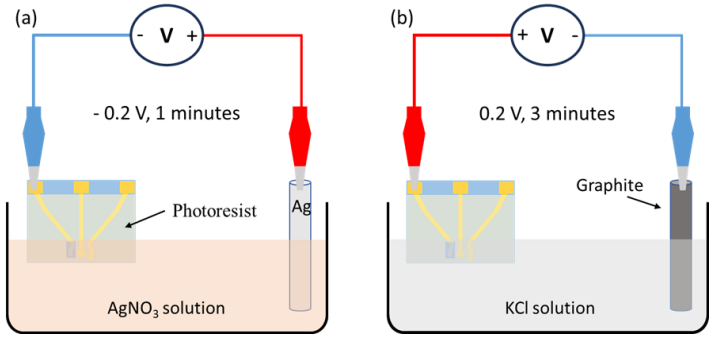


Figure 5.4. The reference electrode fabrication process: (a) silver electroplating; (b) silver chloride coating

Figure 5.5 shows the actual image of electrodes after fabrication.

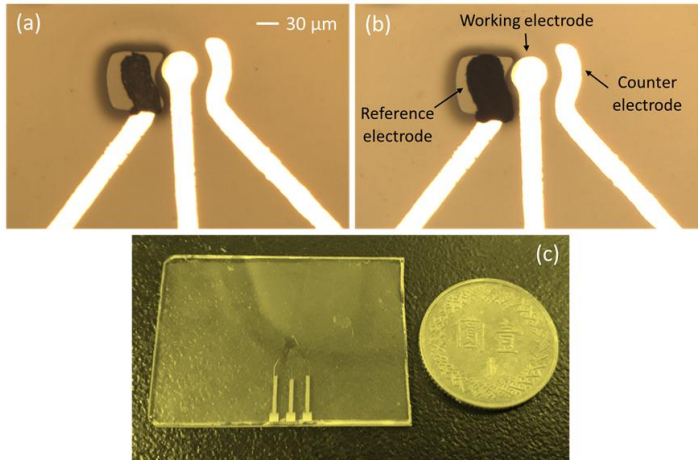


Figure 5.5. The fabricated electrode structure: (a) After silver electroplating; (b) After silver chloride coating; (c) Actual image of electrodes

5.5. Microfluidic channel fabrication process

The microfluidic channel and microfluidic chip were fabricated based on photolithography and soft lithography techniques. Figure 5.7 displays the fabrication result of the proposed chip with the electrochemical electrode positioned inside the main channel of the pre-concentrator.

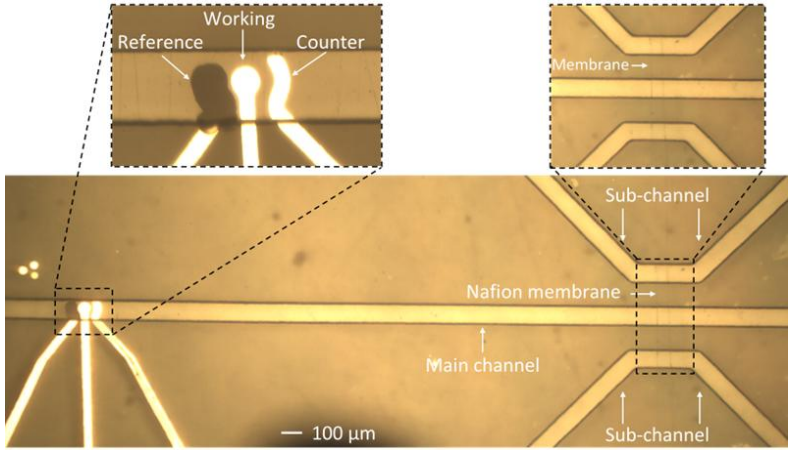


Figure 5.7. The proposed microfluidic chip for BSA pre-concentration and detection after fabrication

5.6. Gold electrode surface functionalization process

After the fabrication of the microfluidic chip, the gold electrode surface underwent functionalization following the process outlined in Figure 5.8. This process aimed to immobilize anti-NSE onto the electrode surface and enable the detection of NSE through specific binding interactions between the antibodies and the target antigen. The process was divided into five main steps, including self-assembled monolayer formation, carboxyl group activation, anti-NSE immobilization, surface blocking, and the binding of NSE.

For the microfluidic chip for BSA protein pre-concentration and detection, the gold electrode surface functionalization process was repeated with anti-BSA. Biotin was used to block the electrode and prevent nonspecific binding between antigens and the electrode surface. Then, the pre-concentration process was used to obtain a high local

protein concentration at the electrode surface and enhance the protein binding efficiency on it.

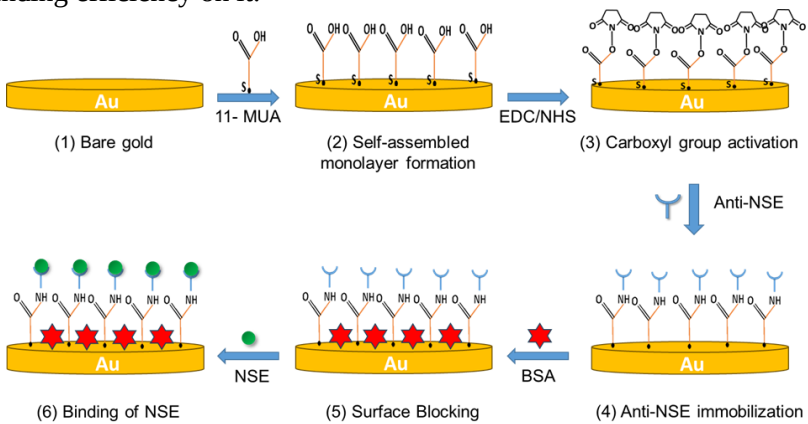


Figure 5.8. Gold electrode surface functionalization process in microchannels for anti-NSE immobilization and NSE protein detection

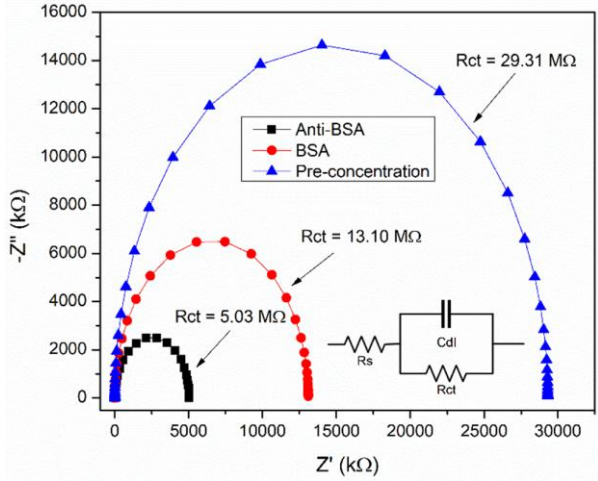


Figure 5.11. The change of EIS signal after the steps of anti-BSA immobilization, BSA incubation, and BSA pre-concentration

5.7. Experimental setup

For the microfluidic chip for NSE detection, The electrode was connected to the Palmsen 4 device according to each implemented NSE concentration to perform EIS measurements in PBS 1X solution.

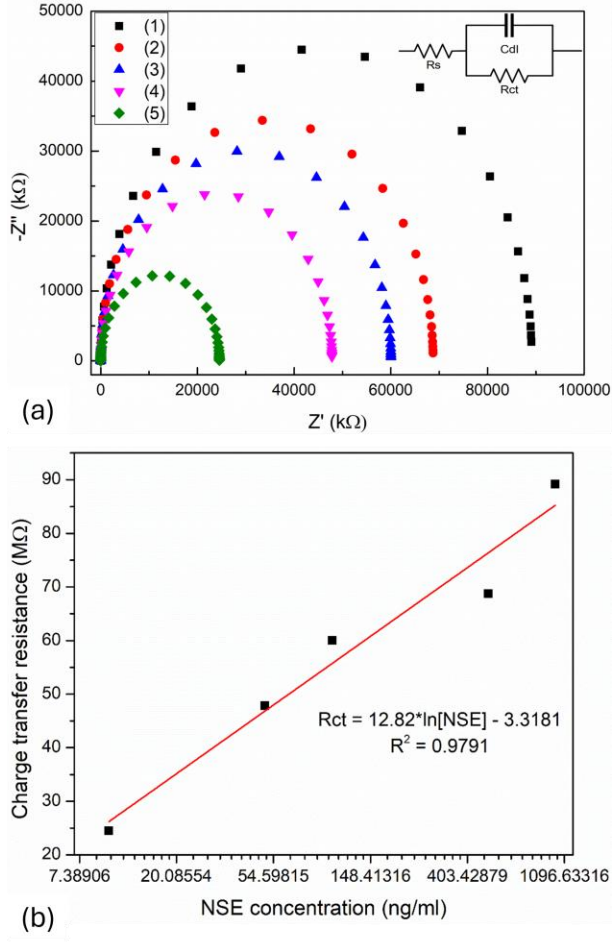


Figure 5.13. (a) The change of EIS signals at different NSE concentrations: (1) 1000 ng/ml, (2) 500 ng/ml, (3) 100 ng/ml, (4) 50 ng/ml (5) 10 ng/ml; (b) The relationship between the charge transfer resistance and the NSE concentration

5.8. Results of BSA protein pre-concentration and detection

For the protein pre-concentration process, the concentration zone was gradually formed after applying the potentials to the ends of the micro-channels. The fluorescence intensity of the protein concentration zone increased rapidly over time. The EIS measurements results are depicted in Figure 5.11, illustrating the EIS signals following the step of anti-BSA immobilization (black curve), after BSA protein pre-concentration (blue curve), and after BSA immobilization for 2 hours without the pre-concentration process (red curve).

5.9. Results of NSE protein detection

For different NSE concentrations, the experimental results show that the EIS signal changed significantly when NSE concentration increased, as shown in Figure 5.13 (a). Figure 5.13 (b) shows the relationship between the charge transfer resistance and NSE concentrations. The result show the LoD of sensor was approximately 1.005 ng/ml, with the standard deviation of 0.0212 MΩ.

Conclusions and future works

In this study, a protein detection system has been successfully developed, presenting a promising platform for point-of-care testing in biomedical diagnostics. This system integrates a microfluidic chip with a protein pre-concentrator, an electrochemical immunosensor, and measuring and control circuits. The pre-concentrator features a dual-gate structure, with a main microchannel for sample actuation and two sub-microchannels to generate depletion regions. These channels are connected through a sub-micron thick ion-selective membrane, formed from Nafion solution using a micro-flow patterning technique. A model of an N-channel junction field-effect transistor was applied to clarify the chip's operational principles. Fabrication of the pre-concentrator relied on a straightforward soft-lithography process using dry film photoresist, eliminating the need for a cleanroom. Impedance within the concentration zone was also analyzed by integrating a gold configuration

inside the main channel, with changes in impedance explained using the Randles model.

The electrochemical immunosensor was designed with a three-electrode configuration, including gold working and counter electrodes, and an Ag/AgCl reference electrode. The working electrode surface was modified to immobilize antibodies, creating the biosensor. Specific antigen-antibody binding on the sensor surface was detected through fluorescence (for BSA-FITC) and electrochemical techniques, such as cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). The combination of the immunosensor with the pre-concentrator in the microfluidic chip enhances both the selectivity and the limit of detection (LoD) of the biosensor. Additionally, a portable device was developed to integrate the microfluidic chip with measuring and control circuits, creating a practical point-of-care device. This device provides voltage potentials for protein pre-concentration and performs electrochemical measurements to detect and quantify protein levels, with results displayed on-screen.

The outcomes demonstrated the system's robust performance and highlighted numerous advantages. This platform holds significant potential for future medical applications, enabling the detection of biological molecules and disease diagnosis via electrochemical and impedance measurements. It promises to advance diagnostic capabilities, particularly for cancer and other biologically complex diseases, paving the way for enhanced disease detection and monitoring.

LIST OF PUBLICATIONS CONCERNING THESIS

1. **Chi Tran Nhu**, Phu Nguyen Dang, Loc Do Quang, Trinh Chu Duc, Chun-Ping Jen, Tung Bui Thanh, "*Development of a microfluidic chip for protein preconcentration using dual gate structure and nanomembrane*", (2023), Microsystem Technologies vol. 29, no. 12, pp. 1757-1767 (WoS, Q3).
2. **Chi Tran Nhu**, Loc Do Quang, Chun-Ping Jen, Trinh Chu Duc, Tung Bui Thanh, "*Development of a Protein Enrichment and Detection Microfluidic Platform based on Ion Concentration Polarization (ICP) and Electrochemical Impedance Spectroscopy (EIS) Techniques*", (2024), IEEE Sensors Letters vol. 8, no. 9, pp. 1-4 (WoS, Q2).
3. **Chi Tran Nhu**, Tuan Vu Quoc, Loc Do Quang, Phu Nguyen Dang, Jen ChunPing, Trinh Chu Duc, Tung Bui Thanh, "*Comparison of faradaic and nonfaradaic impedance biosensors using 2-electrode and 3-electrode configurations for the determination of bovine serum albumin (BSA)*", (2024), Analytical Letters vol. 57, no. 17, pp. 2959–2971 (WoS, Q3).
4. **Chi Tran Nhu**, Tuan Vu Quoc, Loc Do Quang, Phu Nguyen Dang, Son Nguyen Hong, Trinh Chu Duc, Tung Bui Thanh, "*Novel, compact electrochemical and impedance instrumentation*", (2024), Instrumentation Science and Technology, pp. 1-16 (WoS, Q3).
5. **Chi Tran Nhu**, Phu Nguyen Dang, Manh Pham Tien, Trinh Chu Duc, Tung Bui Thanh, Loc Do Quang, "*Functionalization of Carbon Electrode Surface Using Polyaniline and Gold Nanoparticles for Protein Immobilization*", (2024), Analytical Letters, pp. 1–15 (WoS, Q3).
6. **Chi Tran Nhu**, Bui Thanh Tung, Chu Duc Trinh, Nguyen Dang Phu, "*Development of a Non-Enzyme Sensor to Detect Glucose Based on the Modification of Copper Electrode*", (2023), Arabian Journal for Science and Engineering, vol. 49, pp. 9849–9858 (WoS, Q1).
7. **Chi Tran Nhu**, Phu Nguyen Dang, Linh Huynh Thi Thuy, Loc Do Quang, Thuy Nguyen Tran, Trung Le Thanh, Thanh Le Ngoc, Trinh Chu Duc, Tung Bui Thanh, "*An evaluation of a gold surface functionalization procedure for antibody binding and protein detection using 11-mercaptoundecanoic acid (11- MUA)*", (2024), Biomedical

Engineering: Applications, Basis and Communications, vol. 36, no. 02, pp. 2450002 (WoS, Q4).

8. **Chi Tran Nhu**, Anh Phan Hoang, Tuan Vu Quoc, Loc Do Quang, Phu Nguyen Dang, Trinh Chu Duc, Tung Bui Thanh, "*Development of a Low-Cost and Compact Medical Image Reconstruction Platform Based on EIT Technique*", (2024), IETE Journal of Research, vol. 70, no. 08, pp. 7044–7057 (WoS, Q3).
9. **Chi Tran Nhu**, Huynh Thi Thuy Linh, Nguyen Canh Viet, Do Quang Loc, Vu Quoc Tuan, Tran Thi Thuy Ha, Vu Ngoc Trung, Jen Chun-Ping, Chu Duc Trinh, Bui Thanh Tung, Nguyen Dang Phu, "*Development of an immunosensor based on the screen-printed gold electrodes for bovine serum albumin detection*", (2024), International Journal of Nanotechnology (IJNT), Accepted (WoS, Q4).
10. **Chi Tran Nhu**, Trung Vu Ngoc, Jen Chun-Ping, Loc Do Quang, Trinh Chu Duc, Tung Thanh Bui, "*NSE protein detection in a microfluidic channel integrated an electrochemical biosensor*", (2024) Biomedical Physics and Engineering Express Vol 11, No. 1, pp. 1-10 (WoS, Q3)
11. **Chi Tran Nhu**, Nguyen Tran Thuy, Nguyen Cong Huu, Le Thanh Trung, Do Quang Loc, Bui Thanh Tung, "*Development of a Compact System Integrating Pre-Concentrator and Electrochemical Measurements for Protein PreConcentration and Detection*", (2024), in The 10th IEEE International Conference on Communications and Electronics - IEEE ICCE 2024, pp. 178-183.
12. **Chi Tran Nhu**, Loc Do Quang, Chun-Ping Jen, Thuy Nguyen Tran, Huu Nguyen Cong, Trinh Chu Duc, Tung Thanh Bui, "*A Novel Approach to Detect Protein Utilizing the Microfluidic Pre-Concentrator Based on The Impedance Measurement Method*", (2023), in 2023 1st International Conference on Health Science and Technology (ICHST), pp. 1-5.
13. **Chi Tran Nhu**, Phu Nguyen Van, Loan Do Thi, Loc Do Quang, Chun-Ping Jen, Trinh Chu Duc, Tung Bui Thanh, "*Research and Development of A Portable Impedance Measurement System Utilizing AD5941 Analog Integrated Circuit for A549 Lung Cancer Cell Detection*", (2023), in 2023 1st International Conference on Health Science and Technology (ICHST), pp. 1-6.

14. **Chi Tran Nhu**, Phu Nguyen Dang, Hang Tran Thanh, Thom Vu Thi, Loc Do Quang, Tung Bui Thanh, "*A protein preconcentration platform utilizing dual gate structure and ion-selective membrane*", (2022), in 2022 IEEE Ninth International Conference on Communications and Electronics (ICCE), pp. 195-198.
15. **Chi Tran Nhu**, Huynh Thi Thuy Linh, Nguyen Canh Viet, Do Quang Loc, Le Van Chieu, Vu Ngoc Trung, Jen Chung Ping, Chu Duc Trinh, Bui Thanh Tung, "*Detection and quantification of bovine serum albumin using screenprinted gold electrodes and electrochemical measurements*", (2023), in The 8th International Workshop on Nanotechnology and Application (IWNA 2023), pp. 254-257.
16. **Chi Tran Nhu**, Do Quang Loc, Nguyen Dang Phu, Nguyen Cong Huu, Nguyen Tran Thuy, Chu Duc Trinh, Bui Thanh Tung, "*A novel surface functionalization process for carbon electrodes based on the combination of conducting polymer and gold nanoparticles for protein detection*", (2023), in The 8th International Workshop on Nanotechnology and Application (IWNA 2023), pp. 258-261.
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